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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,444	01/29/2002	Wilhelm Hoermann	P67254US0	4260
136	7590	03/22/2004	EXAMINER	
JACOBSON HOLMAN PLLC 400 SEVENTH STREET N.W. SUITE 600 WASHINGTON, DC 20004			DAVIS, DEBORAH A	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/926,444	HOERRMANN, WILHELM
	<b>Examiner</b>	<b>Art Unit</b>
	Deborah A Davis	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_\_.  
 2a) This action is **FINAL**.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-15 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-15 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1.) Certified copies of the priority documents have been received.  
 2.) Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3.) Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                                          |                                                                             |
|--------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                              | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                     | Paper No(s)/Mail Date. _____ .                                              |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|                                                                                                                          | 6) <input type="checkbox"/> Other: _____ .                                  |

## DETAILED ACTION

### ***Allowable Subject Matter***

1. The indicated allowability of claims 1-15 are withdrawn in view of the newly discovered reference(s) to (Structural and Functional Changes in Lung Tissue of Mice Fed with B-Aminopropionitrile Fumarate, L-3-cis-Hydroxyproline, and L-4-cis-Hydroxyproline, Respiration, 1988, vol 54, pages 132-138.). Examiner apologizes for any inconvenience this may cause. Rejections based on the newly cited reference(s) follow.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Popow et al (Respiration, 1988; Vol. 54, pages 132-138).

The claims are broadly drawn to detecting cis-hydroxyproline and derivatives in body fluid or tissue sample by quantitative analysis. Popow et al anticipates the instant claims by disclosing biochemical analyses of 3-cis-hydroxyproline (3cisHP), (4cisHP) and its isomers of hydroxyproline in collagen. The collagen was isolated and hydrolyzed in hydrochloric acid for examination by thin-layer chromatography (page 133, column 2, paragraph 4). Hydrolyzed collagen was added to 20 ul of o-phthalaldehyde, a derivatization reagent, and read on HPTLC plates. Cis-

hydroxyproline and its derivative were measured using 3cisHP and 4cisHP as standards (page 134, column 1, paragraph 1).

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-6 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Sessa et al (Journal of chromatography, 382(1986) 258-263).

Sessa et al anticipates the instant claims in teaching methods to quantify various isomers (derivatives) of hydroxyprolines in body fluid such as urine and plasma through ion-exchange and chromatography pg. 258, paragraphs 1-3). Particular hydroxyprolines reagents used in the instant method are cis-4-hydroxy-L-proline (c-Hyp), trans-4-hydroxy-L-proline, L-proline and others (pg. 259, paragraph 1). The sample that was analyzed was pretreated to allow for sensitive fluorometric detection (eliminate disturbing substances), which is an approach, used to assay hydroxyproline in a sample and purified standards (pg. 258, paragraphs 1-3). Total hydroxyproline was determined by comparing t-4-Hyp/c-4-Hyp of hydrolysates to those generated from standards (pg. 260, paragraph 1).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 7-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sessa et al (Journal of chromatography, 382(1986) 258-263).

The teaches of Sessa et al are set forth above and differ from the instant claims in not pointing out the sequential steps in the process of to determine cis-4-hydroxyproline and a kit to perform the instant process.

However, Sessea et al teaches the reagents in remaining dependent claims which are either specifically described by the references (e.g. detecting cis-4-hydroxyproline, adding an internal standard and hydrolyzing the sample, adding potassium hydroxide, potassium tetraborate and a derivatizing agent used to pretreated the sample to increase sensitivity (eliminate disturbing substances) (claims 7-10) (see pgs. 259-260, reagents and sample preparation, paragraphs 1-5), or constitute obvious variations in parameters which are routinely modified in the art and utilizing known reagents (e.g. adjusting the pH value, using adding cis-3-hydroxyproline as an internal standard, the o-phthalaldehyde reagent and azo dyes such as dabsyl chloride (claims 11-12 and 15) (see pg. 259, paragraphs 1-5 and pg. 262, paragraph 2)). Total hydroxyproline was determined by comparing t-4-Hyp/c-4-Hyp of hydroslysates (pg. 260, paragraph 1).

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Although, Sessa et al does not teach performing the instant process in sequential order, It would have been obvious to one of ordinary skill in the art to use equivalent reagents because they yield equivalent results as that of the instant claimed process. Absent evidence to the contrary, the detection of known hydroxyprolines utilizing known reagents in the instant invention is viewed as routine optimization of the prior art method as described by Sessa et al especially since it has been held that the provision of adjustability, where needed, involves only routine skill in the art. In re Stevens, 101 USPQ 284 (CCPA 1954). With respect to using cis-3-hydroxyproline as an internal standard, as recited in claim 15, it only requires routine skill in the art to use as an internal standard or control a modified form or derivative of hydroxyprolines since it is within the general skill of a worker in the art to select a known material on the basis of its suitability for intended use.

### ***Response to Arguments***

9. Applicant's arguments filed July 28, 2003 have been fully considered and were found to be persuasive and rejection was withdrawn. The particular arguments that were previously found persuasive was found on page 8 in its entirety, wherein Applicant asserted that the reference of Sessa et al did not measure cis-hydroxyproline, but was used as a standard to measure trans-hydroxyproline. But after further review of the reference, it was discovered that total hydroxyproline was determined by comparing the ratio of peak heights of trans-4-hydroxyproline and cis-4-hydroxyproline of hydrolysates to those generated from standards (see Sessa, page 260, lines 1-10). Applicants'

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argument that the Sessa et al reference does not teach measuring the content of cis-4-hydroxyproline in a sample, but taught the content of trans-4-hydroxyproline in tissue samples is not found persuasive. Sessa et al used trans-4-hydroxyproline and cis-4-hydroxyproline standards to measure hydroxyprolines in hydrolysates. Although applicants' argument that there is no single document published about *endogenic cis-hydroxyproline* has ever been published and therefore Sessa et al could not have intended to measure this amine is not found persuasive because the recitation of "endogenic cis-hydroxyproline is not in the instant claims. Applicants' argument of rejection under 103 (a) that the Sessa et al reference does not teach measuring the content of cis-4-hydroxyproline is not found persuasive for reasons aforementioned above. Applicants' argument that the determination of cis-hydroxyproline according to the invention is important for the purpose of following the course of development of the disease and therapeutic measures are not found persuasive because they are not limitations found in the claims.

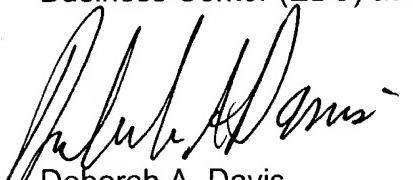
10. No claims are allowed.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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March 19, 2004



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3/20/04